PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Batra et al.	)	
	)	
Serial No.: 09/894,921	)	Examiner:
	)	Sharareh, Shahnam J.
Docket No.: 20243CA	)	
	)	Art Unit:
Filed: June 28, 2001	)	1617
	)	
For: "COMPRESSED TABLET FORMULATION"	)	

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE

Sir:

This communication forms part of a Request for Continued Examination and is in response to the Office Action (final rejection) mailed May 23, 2005, which set a three-month period for response that expires on August 23, 2005. Reconsideration is requested.

The status of the claims is as follows:

Original:	None
Previously presented:	1 and 48-68
Canceled:	2-47

Claims 2-47 were canceled previously. Claims 1 and 48-68 are pending.

Rejection under 35 U.S.C. § 103

Claims 1, 48-53, 55, 57-63 and 65-68 continue to be rejected under 35 U.S.C. § 103(a) as being unpatentable over Makooi in view of Remington or Phipps (US 5,260,073). This rejection is traversed for reasons set forth in Applicants' previous responses and in view of the remarks set forth below.

The Examiner's position is that Applicants' distinction between disintegrants and superdisintegrants is illusory, "because neither the specification nor the art draws a distinction between the scope of the instant disintegrant and superdisintegrants." (see the last 5 lines on page 2 of the instant Office Action). Applicants disagree.

The instant specification does distinguish between disintegrants and superdisintegrants. The specification discloses a compressed tablet comprising both a filler/disintegrant and a superdisintegrant (page 2, lines 14-15) and discloses that the invention contemplates the use, *inter alia*, of any disintegrants and superdisintegrants (page 2, lines 30-31). The specification also discloses that microcrystalline cellulose is the preferred filler/disintegrant and that croscarmellose sodium is the preferred superdisintegrant (page 4, lines 23-24). The presence of both terms in the specification and their use to define and describe different components of the compressed tablet demonstrate that the specification draws a distinction between the terms. Indeed, it would be pointless to include both terms in the specification if there were no distinction between them.

The sentence at page 3, lines 23-27 of the subject specification is susceptible to conflicting interpretations. The sentence reads as follows: "Examples of super-disintegrants include the disintegrants listed above, carboxymethylcellulose sodium, croscarmellose sodium, povidone (sic; should be 'crospovidone'), guar gum, polacrilin (sic; 'polyacrilin') potassium, and pregelatinized starch." The reference to "disintegrants listed above" means the disintegrants previously listed at lines 8-13 on page 3 in the specification. The quoted sentence could be construed to mean that all of the disintegrants listed at lines 8-13 could be used as superdisintegrants, in which case the subject application would make no true distinction between superdisintegrants and disintegrants. This construction, however, is inconsistent with the rest of the specification which clearly indicates that filler/disintegrants and superdisintegrants represent separate and distinct components of the compressed tablet formulation. The correct construction of the quoted sentence is as follows: Of the disintegrants listed at lines 8-13 of page 3 the following are superdisintegrants: carboxymethylcellulose sodium, croscarmellose sodium, crospovidone, guar gum, polyacrilin potassium, and pregelatinized starch. This construction is consistent with and supported by the use of these terms in the rest of the application.

Regarding the Examiner's assertion that the art draws no distinction between disintegrants and superdisintegrants, reference is made to the Rule 132 Declaration of Dr. Conrad S. Winters which accompanies this communication. It is the opinion of Dr. Winters, an expert in pharmaceutical technology, that the art does recognize and draw a distinction between superdisintegrants and disintegrants, that the terms are not used interchangeably in the art. Dr. Winters supports his opinion by an examination of teachings found in Makooi, Remington, and Thibert et al., *J. Pharm. Sci.* 1996, 85, pp. 1255-1258. The Examiner is referred to the Winters Declaration for the details.

Summarizing the foregoing remarks, both the instant specification and the art recognize a distinction between the scope of disintegrants and superdisintegrants. Accordingly, the amount of superdisintegrant (1-5 wt.%) set forth in the instant claims does not overlap with Makooi's teaching of a compressed tablet having 10 wt.% or more superdisintegrant. Furthermore, Makooi clearly directs the person of ordinary skill in the art to efavirenz-containing formulations with $\geq$ 10 wt.% superdisintegrant, and any optimization of Makooi must result in an efavirenz-containing formulation with at least 10 wt.% superdisintegrant. Makooi accordingly does not teach or suggest the claimed compressed tablet compositions containing 1-5 wt.% superdisintegrant.

The disintegrant-superdisintegrant distinction is particularly clear with respect to microcrystalline cellulose and croscarmellose sodium. The specification unambiguously identifies microcrystalline cellulose as a filler/disintegrant and croscarmellose sodium as a superdisintegrant at page 4, lines 23-24. The Winters Declaration pointedly states that croscarmellose sodium is a superdisintegrant and microcrystalline cellulose is not. Accordingly, the "illusory" argument advanced by the Examiner clearly fails with respect to claims 52-56 and 62-68.

The Examiner also asserts that Makooi does not teach away from the instant claims, emphasizing that Makooi contains "no direct statement that low levels of superdisintegrant would not be suitable with efavirenz" (sentence bridging pages 3-4 of the Office Action) and citing *In re Gurley*, 31 U.S.P.Q.2d 1130, 1131-1132 (Fed. Cir. 1994) in support.

Applicants maintain that Makooi teaches away from the instant claims. The critical passage in *In re Gurley* is the following:

> A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.

Makooi directs the skilled artisan to employ 10 wt.% or more of a superdisintegrant in efavirenz-containing tablets and thus is leading the artisan "in a direction divergent from the path taken by" Applicants. The Examiner is correct that Makooi does not directly state that low levels of superdisintegrant are not suitable, but *Gurley* does not require a direct statement in a teaching away; i.e., it is sufficient if the reference "suggests" the path taken by Applicants is "unlikely to be productive". It is known in the art that superdisintegrants are typically effective at a low level (i.e., less than 10 wt.%). Makooi itself says so at col. 1, lines 54-57. Nonetheless, Makooi tells the person of ordinary skill to use at least 10 wt.% superdisintegrant in efavirenz compositions.

Makooi is clearly suggesting to the skilled artisan that superdisintegrants are not to be used in efavirenz-containing compositions at low levels. Thus, Makooi is urging the skilled artisan to follow a path divergent from that of Applicants and is teaching away.

Neither Remington nor Phipps cures the deficiencies of Makooi. As set forth in previous communications, Remington provides a general description of tablet preparation and tablet ingredients that in no way contradicts Makooi's direction to the person of ordinary skill in the art to employ 10 wt.% or more of a superdisintegrant in efavirenz solid dosage forms. The Examiner has noted that Phipps was offered only to "elaborate how the state of the art characterizes superdisintegrants and disintegrants". (See page 3, lines 3-4 of the instant Office Action.) As discussed in the response filed February 24, 2005 and as mentioned in the Winters Declaration, the failure in Phipps to make a distinction between disintegrants and superdisintegrants does not mean none is recognized in the art. It merely means that the distinction is not important in the context of Phipps' tablet formulations.

Withdrawal of the rejection under section 103(a) is requested in view of the foregoing remarks.

Declaration under 37 C.F.R. 1.132

Assuming strictly for the sake of argument that the claims were prima facie obvious, then the claims are patentable over Makooi and Remington or Phipps in view of the unexpected results set forth in the Rule 132 Declaration of Munir Alwan Hussain for the reasons set forth in previous communications (see, e.g., the amendment filed February 24, 2005). The Examiner has asserted that the Hussain Declaration is sufficient to overcome the rejection of claims 54, 56 and 64 but is not commensurate in scope with the other claims. The Examiner's interpretation of the results set forth in the Declaration is unreasonably narrow. It is Applicants' position that the evidence of unexpected results provided in the Declaration can be extrapolated to and is representative of the entire class of tablets embraced by the claims as amended herein. In particular, those claims reciting the same ingredients as employed in the tests set forth in the Declaration -- claims 52-56 and 62-68 -- are commensurate in scope with the Hussain Declaration.

Claim Objection

Claims 54, 56 and 64 have been objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. (Note: In some places the Office Action states claim 62, not claim 64, is objected to, but this is believed to be an inadvertent error.) The Examiner's invitation to rewrite the claim in independent form is declined, because it is believed that the rejection of the base claim should be withdrawn for the reasons set forth above. Withdrawal of the objection is accordingly requested.

The application is believed to be in condition for allowance and passage to issue is requested. The Examiner is invited to telephone the undersigned should any minor matters need to be resolved before a Notice of Allowance can be mailed.

Respectfully submitted,

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